AXITINIB (INLYTA®)
for second line treatment of mRCC

NHS Northern Cancer Alliance

DRUG ADMINISTRATION SCHEDULE

Day	Cycle length	Drug	Daily Dose	Route	Schedule
Days 1 to 28	4 weeks	**Axitinib**	5 mg *(see dosing below)	Oral	Twice daily

Axitinib is available as 7mg, 5mg, 3mg and 1mg tablets, which may be taken with or without food, swallowed whole with a glass of water.

APPROVED INDICATIONS
NICE TA333
Axitinib is recommended as an option for treating adults with advanced renal cell carcinoma after failure of treatment with a first-line tyrosine kinase inhibitor or a cytokine.

DOSING INFORMATION
- After 4 weeks, for patients who tolerate this dose with no severe adverse reactions and whose blood pressure remains ≤ 150/90 mmHg without the need for anti-hypertensives, the dose may be increased to 7mg twice daily.
- Subsequently, using the same criteria above, patients who tolerate the 7mg twice daily dose without the need for an antihypertensive may have their dose increased to a maximum of 10mg twice daily.

DOSE FREQUENCY
Clinical review 2 weeks after starting, then every 4 weeks continue for as long as there is clinical benefit, or unacceptable toxicity.

ANTI-EMETICS AND SUPPORTIVE MEDICINES
Loperamide 2mg prn (max 16mg in 24 hours) for diarrhoea as required
Emollients (for skin rash) as required

INVESTIGATIONS / MONITORING REQUIRED
- FBC every 4 weeks
- LFTs every 4 weeks
- U&Es every 4 weeks
- Blood pressure – weekly for 1st cycle then every 4 weeks.
- Thyroid function – baseline, then every 3 months
- Urinalysis for proteinuria – baseline, then every 3 months

REVIEW BY CLINICIAN
Review at each cycle as appropriate

NURSE / PHARMACIST LED REVIEW
Each cycle as applicable according to local protocols

ADMINISTRATION NOTES
- Grapefruit and grapefruit juice should be avoided whilst on axitinib treatment.
- Diarrhoea is common, so provide loperamide for new patients, and ask them to contact the team if there is an increase of 4-6 stools per day over baseline
- Axitinib is metabolised primarily in the liver by CYP3A4/5. Concomitant use of enzyme inducers (e.g. dexamethasone, phenytoin, St John's wort) with axitinib should be avoided, as this may increase the risk of therapeutic failure.

- If co-administration with enzyme inducers is required, axitinib should be gradually titrated up as tolerated. If the interacting medication is discontinued, the dose should return to the previous dose.
- Co-administration of axitinib with CYP3A4/5 inhibitors (e.g. itraconazole, clarithromycin, erythromycin, grapefruit juice) should also be avoided. If a strong inhibitor must be co-administered, a dose decrease of axitinib to approximately half the dose (e.g. the starting dose should be reduced from 5mg twice daily to 2mg twice daily) is recommended. If co-administration of the strong inhibitor is discontinued, a return to the axitinib dose used prior to initiation of the strong inhibitor should be considered.
- Patients should be advised to apply moisturiser to their hands and feet regularly throughout the treatment, and to minimise activities that put pressure on feet or hands if they start to develop sore hands or feet.

MAIN TOXCITIES

- Palmar-plantar erythrodysaesthesia (hand-foot syndrome)
- Proteinuria
- Fatigue
- Diarrhoea
- Hypothyroidism
- Hypertension
- Dysphonia (Hoarseness)
- Haemorrhage
- GI Perforation
- Arterial embolic and thrombotic events (e.g. MI, TIA, stroke).

DOSE MODIFICATIONS

Management of some adverse drug reactions may require temporary interruption or dose reduction or therapy. When dose reduction is necessary, axitinib may be reduced to 3mg twice daily, and further to 2mg twice daily.

Haematological Toxicity

Temporarily delay if ANC < 1.5 or Platelets < 100 until counts recovered.

Hypertension

Blood pressure should be well controlled before starting axitinib. If hypertension develops, it should be treated and monitored closely until stabilised. If the hypertension is persistent despite the use of anti-hypertensives, the axitinib dose should be reduced.

If the patient develops severe hypertension, axitinib should be stopped until the patient is normotensive. Axitinib may be re-started, with close monitoring, at a lower dose.

If axitinib is interrupted for any reason, patients receiving antihypertensive medicinal products should be monitored for hypotension

Thyroid dysfunction

Manage according to standard medical practice. Axitinib treatment may continue.

Proteinuria

For patients who develop moderate to severe proteinuria (≥ 2+ on dipstick, or > 1g/24 hours), reduce the dose or temporarily interrupt axitinib. Axitinib should be discontinued if the patient develops nephrotic syndrome.

Dysphonia
Includes sensation of lump in throat, difficulty swallowing, sore throat, hoarse voice and chronic throat clearing. This can be intermittent, but usually resolves after 1-2-day treatment interruption. Consider dose reduction if symptoms are severe or troublesome.

Skin Toxicity
Grade 3 hand-foot syndrome may require a break in treatment until resolved to Grade ≤ 1. The patient should be advised to moisturise their hands and feet regularly, and to keep them cool. Once symptoms have resolved to ≤ Grade 1, axitinib may be re- introduced at a reduced dose.

Hepatic Impairment
In clinical studies, the systemic exposure to axitinib was approximately two-fold higher in subjects with moderate hepatic impairment (Child-Pugh class B), so a dose decrease to 2mg twice daily is recommended when administering axitinib to these patients.
Axitinib is not recommended in patients with severe (Child-Pugh class C) hepatic impairment.

Renal Impairment
No dose adjustment is required in renal impairment however there is very little data available in patients with a creatinine clearance of <15 ml/min.

EXTRAVASATION Not Applicable

TREATMENT LOCATION
Cancer Centre or Cancer Unit where there is an Oncologist with a specialisation in Renal Cancer patients as appropriate.

REFERENCES
1. Pfizer - SPC Inlyta, https://www.medicines.org.uk/emc/product/7947 Last updated 3/9/12
2. NICE, TA 333 Axitinib for treating advanced renal cell carcinoma after failure of prior systemic treatment, https://www.nice.org.uk/guidance/ta333

DOCUMENT CONTROL

Document Title:	AXITINIB (INLYTA®) for second line treatment of mRCC		
Document No:	NCDF03	**Current Version:**	1.2
Reviewer:	Chris Beck Chemotherapy Pharmacist Northern Cancer Alliance	**Date Approved:**	13.03.18
Approved by:	Steve Williamson Consultant Pharmacist Northern Cancer Alliance	**Due for Review**	13.03.21
Summary of Changes	1.1	Document approved.	
	1.2	NICE approval updated, parameters updated from Chemocare.	